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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,441	04/15/2004	Patrick M. Hughes	17686 (OCU)	1056

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EXAMINER	
NAVARRO, ALBERT MARK	

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1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,441	HUGHES ET AL.	
	Examiner	Art Unit	
	Mark Navarro	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17-20,23-25,27,29-31 and 33-39* is/are pending in the application.

4a) Of the above claim(s) *23,29 and 34-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,17-20,24,25,27,30,31,33 and 37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment filed November 12, 2008 has been received and entered. Claims 16, 21-22, 26, 28 and 32 have been cancelled, and new claims 34-39 have been added. Accordingly, claims 1-15, 17-20, 23-25, 27, 29-31, and 33-39 are pending in the instant application.

Election/Restrictions

Newly amended and newly submitted claims 23, 29 and 34-36 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claims 23, 29 and 34-36 are directed to a biodegradeable neurotoxin comprising an acidity regulating component, wherein the component comprises a monomer and an oligomer derived ***from a different biodegradable polymer***. (Emphasis added). This is mutually exclusive from the originally presented claims which set forth that the acidity regulating component compised a monomer and an oligomer derived from the same biodegradable polymer. As set forth in MPEP 806.04(f) restriction between mutually exclusive species is proper.

Note claims 23 and 29 were examined in the previous office actions, however they both depended upon claim 1 which recited that the monomer and the oligomer derived from the same biodegradable polymer. Applicants claims remain improper as an attempt to limit the oligomer to a "second biodegradable polymer" does not further limit the parent claim 1, which sets forth that "the monomer and the oligomer are derived

from the ***same*** biodegradable polymer." Applicants new claims 34-36 do not depend on claim 1, and are thus proper, however, they are restricted out from further consideration as being a mutually exclusive combination from the originally presented claims.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 23, 29, and 34-36 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Objections

1. The objection of claims 7 and 11 for failing to end with the punctuation mark of a period "." is withdrawn in view of Applicants amendment.

2. The rejection of claims 21 and 23 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in view of the cancellation of claim 21 and the withdrawal of claim 23 due to the restriction requirement set forth above.

3. The objection of claim 29 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in view of the restriction requirement set forth above.

4. The objection of Claim 32 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in view of the restriction requirement set forth above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. The rejection of claims 1-15, 17-20, 24-25, 27, 30-31, and 33 under 35 U.S.C. 102(b) as being anticipated by Donovan et al (US Patent Number 6,506,399) or Donovan et al (US Patent Number 6,312,708) is maintained.

Additionally, this rejection is applied to newly added claims 37-39.

Applicants are asserting that the current limitation in claim 1 “an acidity regulating component effective in establishing in vivo a pH in the vicinity of the neurotoxin component associated with the implant of less than about 7” carries patentable weight and must be considered. Applicants further assert that monomers and oligomers of acidity regulating component in accordance with the presently claimed invention typically degrade at a relatively faster rate than the polymer or generate acid functionalities at a faster rate, thus they are effective in maintaining an acidic

environment or microenvironment of a neurotoxin implant. Applicants further assert that Donovan et al supplies polymers but not monomers and oligomers initially furnished in addition to biodegradable polymers. Applicants finally assert that Donovan do not teach an acidity regulating component comprising a monomer and an oligomer derived from a different biodegradable polymer.

Applicants arguments have been fully considered but are not found to be fully persuasive.

First, Applicants are asserting that the current limitation in claim 1 “an acidity regulating component effective in establishing in vivo a pH in the vicinity of the neurotoxin component associated with the implant of less than about 7” carries patentable weight and must be considered. However, this limitation has been given patentable weight. Applicants claim language sets forth that the acidity regulating component comprises a monomer and an oligomer derived from the same biodegradable polymer. Donovan et al disclose of the same biodegradable polymers as claimed, e.g., PLGA. (See claims and paragraph 84 of ‘399). Furthermore, the PLGA polymer disclosed by Donovan inherently ***comprises*** oligomers and monomers of PLGA, as each are building blocks of the polymer molecule. Furthermore, oligomers and monomers of PLGA will be spontaneously generated in vivo as the polymer breaks down.

It is noted that Donovan does not use PLGA "for maintaining in vivo pHs of less that about 7." However, “[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not

render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition by a person of ordinary skill in the art before the critical date and allowing expert testimony with respect to post-critical date clinical trials to show inherency); see also Toro Co. v. Deere & Co., 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004). "[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention."); Abbott Labs v. Geneva Pharms., Inc., 182 F.3d 1315, 1319, 51 USPQ2d 1307, 1310 (Fed.Cir.1999).

Second, Applicants further assert that monomers and oligomers of acidity regulating component in accordance with the presently claimed invention typically degrade at a relatively faster rate than the polymer or generate acid functionalities at a faster rate, thus they are effective in maintaining an acidic environment or microenvironment of a neurotoxin implant. However, the rate of "degradation" is not a limitation set forth in the claims, and consequently cannot be used to distinguish over the composition disclosed by Donovan et al.

Third, Applicants further assert that Donovan et al supplies polymers but not

monomers and oligomers initially furnished in addition to biodegradable polymers. However, Applicants are again respectfully directed to their own claim language which recites "wherein the acidity regulating component ***comprises*** a monomer and an oligomer derived from the same biodegradable polymer." (Emphasis added). The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., > Mars Inc. v. H.J. Heinz Co., 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004) ("like the term comprising,' the terms containing' and mixture' are open-ended.").< Invitrogen Corp. v. Biocrest Mfg., L.P., 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) ("The transition comprising' in a method claim indicates that the claim is open-ended and allows for additional steps."); Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts"). >In Gillette Co. v. Energizer Holdings Inc., 405 F.3d 1367, 1371-73, 74 USPQ2d 1586, 1589-91 (Fed. Cir. 2005), the court held that a claim to "a safety razor blade unit comprising a guard, a cap, and a group of first, second, and third blades" encompasses razors with more than three blades because

the transitional phrase "comprising" in the preamble and the phrase "group of" are presumptively open-ended. "The word comprising' transitioning from the preamble to the body signals that the entire claim is presumptively open-ended." Id. In contrast, the court noted the phrase "group consisting of" is a closed term, which is often used in claim drafting to signal a "Markush group" that is by its nature closed. Id. The court also emphasized that reference to "first," "second," and "third" blades in the claim was not used to show a serial or numerical limitation but instead was used to distinguish or identify the various members of the group. Accordingly, the recitation of "comprises" specifically allows for the monomers and oligomers to be present in the form of a polymer.

Finally, Applicants assert that Donovan do not teach an acidity regulating component comprising a monomer and an oligomer derived from a different biodegradable polymer. However, this limitation has been withdrawn from further consideration as directed to a non-elected invention by original presentation, and consequently cannot be used to distinguish over the prior art.

For reasons of record as well as the reasons set forth above, this rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the

> subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. The rejection of claims 1-15, 17-20, 24-25, 27, 30-31, and 33 under 35 U.S.C. 103(a) as being unpatentable over Donovan et al in view of Schwendeman et al is maintained.

Additionally, this rejection is applied to newly added claims 37-39.

Applicants are asserting that the whole aim of Schwendeman et al was to prevent acid degradation of a polymer such as PLGA. Applicants assert that the examiner has picked and chosen from the reference only that which will support a given position to the exclusion of other parts necessary to fully appreciate what such reference fairly suggests to one skilled in the art.

Applicants arguments have been fully considered but are not found to be fully

persuasive.

Applicants assert that the whole aim of Schwendeman et al was to prevent acid degradation of a polymer such as PLGA. However, Applicants will note that this is not a 102 rejection, rather a 103 based on the combination of teachings of Donovan et al and Schwendeman et al. One cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co. Inc.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Indeed, the combination of Donovan et al and Schwendeman et al set forth the combined rationale for producing such a composition. Donovan et al specifically teach that botulinum toxin implants are extremely susceptible to denaturation due to heat and alkaline (non acidic) conditions. (See claims and summary paragraph 38). When combined with a teaching by Schwendeman et al that "monomers or oligomers can produce acidic microclimate even before polymer degradation occurs" one of ordinary skill in the art would readily appreciate adding monomers or oligomers to botulinum toxin implants to maintain them in a more stable acidin microclimate, thereby avoiding the harsh denaturing alkaline conditions when monomers and oligomers are not present. It is proper to "take account of the inferences and creative steps that a person of ordinary skill in the art would employ." KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 1741, 82 USPQ2d 1385, 1396 (2007). See also id. At 1742, 82 USPQ2d 1397 ("A person of ordinary skill is also a person of ordinary creativity, not an automaton.").

The claims are directed to a biodegradable neurotoxin implant, comprising a neurotoxin component associated with a biodegradable polymer component and an acidity regulating component for establishing in vivo a pH in the vicinity of the neurotoxin component associated with the implant of less than about 7, wherein the acidity regulating component comprises a monomer and an oligomer derived from the same biodegradable polymer.

Donovan et al (US Patent Number 6,506,399) teaches a biodegradable botulinum toxin implant and the importance of maintaining an acidic environment for the controlled release of botulinum toxin in vivo. Donovan et al further teach that pure botulinum toxin is labile and the botulinum toxin type A complexes are extremely susceptible to denaturation due to heat and alkaline conditions. (See claims and summary paragraph 38).

Donovan et al does not teach of acidity regulating components comprising a monomer and an oligomer of a polymer.

Schwendeman et al (US Publication 2002/0009493) teach of methods for inhibiting the inactivation of biologically active agents in biodegradable polymeric delivery systems. Schwendeman et al further teach that the presence of "monomers or oligomers can produce acidic microclimate even before polymer degradation occurs." (See paragraph 84). Schwendeman et al reported these findings with the polymer PLGA. (Again, see paragraph 84).

Given that 1) Donovan et al have taught of biodegradable neurotoxin implants having a biodegradable polymer and the need for keeping botulinum toxin at an acidic

pH to prevent denaturation, and that 2) Schwendeman et al has taught of using monomers or oligomers of PLGA to produce an acidic microclimate even before degradation of the polymer occurs, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have incorporated the monomers or oligomers of PLGA to create an acidic environment for the botulinum toxin neurotoxin implant as taught by Donovan et al. One would have been motivated to produce such a composition in light of the teaching by Donovan et al that botulinum toxin is extremely susceptible to denaturation due to alkaline conditions.

For reasons of record, as well as the reasons set forth above, this rejection is maintained.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark Navarro/
Primary Examiner, Art Unit 1645
January 26, 2009